

IN THE CLAIMS

This listing of claims replaces all prior versions, and listings, in this application.

Claims 1-14 (canceled)

15. (previously presented) A method of screening for interaction of an enzyme with at least one of a set of linear peptides in solution, wherein said set is provided in each of a complementary pair of combinatorial libraries comprised of the same number of different peptides, referred to as primary library L1 and a secondary library L2, the method comprising:

- (a) forming said primary library L1 and said secondary library L2 by placing mixtures of different peptides separately each into individual wells positioned on plates, wherein any two peptides which are found together in one mixture of L1 are not found together in any one mixture of L2;
- (b) applying said enzyme to said wells; and
- (c) screening for an interaction of said enzyme with at least one peptide in (i) a well of the plates of L1 and (ii) a well of the plates of L2, to identify said at least one peptide interacting with the enzyme from positions of said well of L1 and said well of L2 where such interaction occurs;

wherein said peptides are each comprised of at least four natural or non-natural amino acid residues B, C, D or E of formula —B_b—C_c—D_d—n(E_e)—;

wherein b, c, d, e are the number of individual B, C, D and E residues respectively and n is any integer between 1 and 4 inclusive;

wherein the mixtures in all wells of the plates of L1 is comprised of all variations of two amino acid residues selected from B, C, D or E which result in a soluble peptide, and each well of the plates of L1 contains a unique pair of the other two amino acids selected from B, C, D or E;

wherein the mixtures in all wells of the plates of L2 is comprised of all variations of said other two amino acids which result in a soluble peptide, and each well of the plates of L2 contains a unique pair of said two amino acids; and

wherein said mixtures are placed separately each into individual wells positioned on plates in a format complying with general deconvolution formulae in which:

- i) $ns = \frac{Rp.Cp.np}{Rs.Cs}$
- ii) $k = b.c.d.np.e$
- iii) $k = X.N.np$
- iv) $N = Rp.Cp$
- v) $k = X.Rp.Cp.np$
- vi) $b.c.d.e = X.Rp.Cp$
- vii) $Cp.e = X$
- viii) $Rp.e = X$, if $Rp=Cp$

and

np = number of plates in the primary library L1

ns = number of plates in the secondary library L2

Rp = number of primary rows

Rs = number of secondary rows

Cp = number of primary columns

Cs = number of secondary columns

k = number of combinations of peptides

N = number of wells on a plate

X = number of peptides per well.

16. (previously presented) A method according to claim 15, wherein said enzyme is a peptidase or protease.

17. (previously presented) A method according to claim 15, wherein said enzyme is a cysteine protease.

18. (previously presented) A method according to claim 16, wherein the wells of the plates of L1 contain all variations of amino acid residues B and E and each well of the

plates of L1 contains unique pairs of C and D; and the wells of the plates of L2 contain all variations of amino acid residues C and D and each well of the plates of L2 contains unique pairs of B and E.

19. (previously presented) A method according to claim 15, wherein

$$np = 4$$

$$ns = 16$$

$$Rp = 8$$

$$Rs = 4$$

$$Cp = 10$$

$$Cs = 5$$

$$k = 6400$$

$$N = 80$$

$$X = 20.$$

20. (previously presented) A method according to claim 15, wherein said peptides each consist of at least four natural or non-natural amino acid residues B, C, D or E of formula —Bb—Cc—Dd—n(Ee)—.